EDITORIAL COMMENT †

SYNERGIC THEORY OF ANAPHYLAXIS

According to data recently reported by Kellaway and Trethewie,[1] of the Institute for Medical Research, Melbourne, Australia, there are two independent reacting mechanisms in acute anaphylaxis: (a) an explosive formation or liberation of histamine or histamine-like substances by the tissue proteins, followed by (b) the liberation of a second ergin or toxic factor derived from the tissue lipids.

Discovery of this hitherto unsuspected lipoidal anaphylatoxin was a by-product of researches on the pharmacodynamics of certain snake venoms. It has long been known[2] that in cobra-venom hemolysis, for example, laking of the red blood cells is not due to a direct action of the venom, but to its immediate action on lecithin. The lipolytic enzymes of the venom lead to the formation of a lecithin split-product ("lysocithin") which is directly hemolytic. This active hemolysin can be readily produced by the action of cobra venom on egg yolk or other lecithin containing materials *in vitro*. Chemically the "lysocithin" is a lecithin molecule robbed of one of its oleic acid radicles. The Australian investigators found that in a similar way contraction of smooth muscles under the influence of certain snake venoms is also due to the formation of certain smooth-muscle stimulating split-product of tissue lipids. This active split product or lipoergin can also be produced *in vitro* by the action of venom on egg yolk. The substance is soluble in acetone, by means of which it can be separated from "lysocithin."

The smooth-muscle contracting properties of this lipo-ergin are quite different from those of histamine. Tested on the isolated guinea-pig jejunum, for example, histamine produces an immediate maximum contraction with relatively prompt recovery. The lipo-ergin, in contrast, causes a slowly developing contraction only after a fairly long latent period, with a very sluggish recovery. For this reason the Australian biochemists refer to the lipo-ergin as a "slow-reacting smooth-muscle-stimulating substance" or "SRS."

Histamine and lipo-ergin apparently act on different elements in the smooth muscle. This is shown by a selective suppression of one reactivity by certain therapeutic agents. Exposure to B. welchii toxin, for example, will almost completely desensitize a smooth muscle to the lipo-ergin, without appreciably reducing its histamine sensitivity. Poisoning with relatively large doses of histamine may cause certain smooth muscles to react to further doses by relaxation, whereas its lipo-ergin sensitivity is practically unaltered. Applying these and other selective depressants, Kellaway and Trethewie found that the typical anaphylactic response of smooth muscle can be analyzed into two components. First there is an initial histamine-like response. In this there is afterwards superimposed a typical slow lipo-ergic tetanus. Therapeutic blockade of both histamine and lipo-ergic sensitivity will prevent anaphylactic smooth muscle contractions, though suppression of either one of these is ineffective.

About ten years ago it was shown by Bartosch[3] that if sensitized guinea pig lungs are perfused with Tyrode's solution plus homologous antigen, the hypersensitive tissues liberate histamine into the perfusion fluid. The Australian investigators found that this liberation is mainly confined to the initial stages of the perfusion. Thus in one of their tests, the first two 5 c.c. samples of the perfusion fluid contained a total of about 2.5 *gamma* histamine. There was a fairly large trace of histamine in the third sample, after which the samples became histamine-free. Analysis of the same samples showed no lipo-ergin in the first sample. Moderate amounts appeared in the second and third samples, with gradually diminishing amounts in subsequent samples.

The evidence, therefore, seems complete that there are two superimposed pathologic internal secretions in acute anaphylactic shock, both of which must be taken into account in any logical attempt at anti-anaphylactic therapy. The Australian physiologists believe that it is reasonable to assume that the same or a similar toxic lipoidal split-product may play an important rôle in other shock-like conditions, particularly in traumatic shock and superficial burns.

P. O. Box 51.

W. H. MANWARING,
Stanford University.

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† This department of CALIFORNIA AND WESTERN MEDICINE presents editorial comments by contributing members on items of medical progress, science and practice, and on topics from recent medical books or journals. An invitation is extended to all members of the California Medical Association to submit brief editorial discussions suitable for publication in this department. No presentation should be over five hundred words in length.

MALPRACTICE INSURANCE*

At one time or another, during the last thirty years, a considerable number of insurance companies have engaged in writing physicians' professional liability insurance in California. That the business has not generally been profitable is evidenced by the fact that most of these companies no longer offer this coverage. The high incidence of malpractice claims and suits explains why this business is regarded as undesirable, even though the cost to the insured has increased

* Fourth of a series of articles on Malpractice Prophylaxis (Article I, in July issue, on page 7. Article II, in August, on page 121. Article III, in September, on page 173.)

considerably and limitation has been placed, by at least one company, on the amount of coverage offered.

Several factors have brought about increased insurance costs in this field. For example, the average trial time of malpractice suits has lengthened, and the cost of obtaining medical expert testimony has increased. During the past year several cases have required more than three weeks to try, and one case was in trial for more than six weeks. As must be expected when this type of trial is so absurdly long, the jury in the latter case was unable to agree upon a verdict.

Many busy physicians of great experience and the highest standing in their respective fields offer to, and actually do testify gratis in defense of their fellow practitioners; but, unfortunately, there are also "professional" medical expert witnesses who, if requested to testify for the defendant in an unjustified malpractice action, demand a large per diem fee.

Certain other factors contribute to the high cost of malpractice insurance in California; for it must be realized that, in the final analysis, the physician pays all of these costs. In those cases wherein there are multiple defendants, not uncommonly each of the two or more co-defendants is insured by a different company, or in Lloyds through different underwriters. Such a situation results in a duplication of legal costs, and certainly does not tend to increase the harmony and efficiency of the defense. Moreover, some carriers or their representatives utilize general insurance investigators and adjusters to investigate malpractice claims. These claims are not suitable for such handling. Finally, in too many cases malpractice insurance has been used as a sort of "come-on" to bring other business into the insurance company's office. This practice naturally obviates any reasonable or proper selection of risks.

In the final analysis, however, it is the physician himself who is responsible not only for the unsatisfactory insurance condition, but also for the continuing existence of the vicious malpractice situation. He is responsible, because he has been satisfied to pay his premiums and sit back complacently, doing nothing until he becomes the target for a malpractice claim. The physician must be brought to realize that his money payment is only a part of his insurance premium; the much more important part is his contribution of time, of study, and of putting into effect all possible measures to safeguard himself and his confreres.

The physician has apparently failed to understand that the problem of malpractice is *his* problem. Why should he expect the insurance companies to do his job for him? Why should the insurance companies care how high the premium rates climb, unless they become so high that the physician has to carry his own insurance? Representatives of some of the companies have so expressed themselves: they have said that if the physicians do not take an active part in their own behalf, conditions can be expected to continue along the present unsatisfactory course. Such a course will lead, in effect, to increased rates, decreased coverage, and a constantly increasing number of those regarded as uninsurable risks.

Few physicians, even when a malpractice claim is made or suit brought against them, take an active and intelligent interest in the matter. By way of illustration, within the last few months a physician who was served with a complaint and summons did nothing in regard to the matter for approximately sixty days. He did not notify his insurance carrier. Of course, in the meantime a judgment by default was taken.

The fact that a physician might reasonably expect the insurance carrier to make an immediate and thorough study of a claim does not excuse the physician for apathy and seeming indifference. Such a claim is a serious threat to him. He should insist upon its being handled immediately and efficiently. He must not lose sight of the fact that the attorney supplied by the insurance carrier is employed and paid by the carrier. These attorneys are very generally of the highest ability and integrity, but it is obvious that, to some extent, there may be divergence of interests on the parts of the insured and the insurer. The physician should make himself cognizant of every step in the development of his case.

Suggestions:

1. There should be a reasonable selection of risks, so as to eliminate the physician who will not realize his vulnerability and take the available precautions.

2. Reports should be required from insurance carriers so that the exact cost of malpractice insurance may be known to the medical group. This procedure would permit an equitable rate; moreover, it would thus be possible and proper to assess proportionate rates in respect to risks and cost in the various fields of medical practice.

3. Immediate and expert handling of all malpractice claims should be demanded.

4. Meritorious claims should be settled out of court.

5. The nonmeritorious claim should be fought to the last resort, and no claim should be settled because of its "nuisance" value.

6. The highest standard of defense should be demanded. The defense should be concentrated whenever several defendants are involved, thus reducing the cost and increasing the unity, harmony, and efficiency of the defense.

7. Physicians appearing as expert witnesses in malpractice cases should do so without fee, unless expense is incurred or special study or investigation is required. No charge should be made for appearing either on behalf of the defendant or the plaintiff. If both these things were done, the insurance costs of the defendant would be dras-

tically reduced, and subsidized, biased, and highly-colored testimony would be eliminated.

6777 Hollywood Boulevard.

LOUIS J. REGAN,
Los Angeles.

BIOLOGICAL SPECIFICITY OF RENIN

It is currently reported by Braun-Menendez[1] and his coworkers of the University of Buenos Aires, that renin, the recently demonstrated internal secretion from the ischemic kidney,[2] is species-specific, requiring a species-specific coenzyme for its activation. If so little or no therapeutic effect can be predicted from the use of lower animal renins in human medicine.

It was shown by Kohlstaedt and Page[3] that this hypertension-precursor is activated by certain serum globulins, giving rise to a thermostable pressor substance, for which the name "angiotonin" has been suggested.[4] In the hands of the Argentine endocrinologists globulin activation is readily effected in vitro by the action of horse serum, swine serum, ox serum or dog serum on swine renin. Swine renin, however, is not activated by human serum globulins. In order to bring about human activation human renin must be substituted.

This unsuspected species-specificity of the kidney enzyme (or of the serum activator) suggests that swine renin would be therapeutically inert in the human body. It also throws doubt of the current presumptive therapeutic value of certain other endocrine products, some of which conceivably may also require species-specific activation.

P. O. Box 51.

W. H. MANWARING,
Stanford University.

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The Home Front—Challenge to Medicine

Obviously, those in authority—the President, the Congress, and the Supreme Court—are weighing the evidence and are daily making the decisions that will determine the structure and functional changes, which, in turn, will guide our political and social future. Into the newer political and social structure of the country, organized medicine will necessarily have to fit its plans and concepts. . . .

The war may serve in this country as a substitute for those revolutionary mass movements which have been the usual manifestation of major social transition abroad. . . .

There is now developing a distinct challenge, as we have attempted to show editorially in preceding issues of the *Journal*, to the resourcefulness and fluidity of organized medicine. It must supply doctors for the armed forces and is doing it; it must implement what we hope will be an expanding program of industrial medical service from a relatively small reservoir of physicians; it must study and meet the problem of adequate medical and hospital service to areas and communities which need it with the thought in mind that every community without private care is an argument for public medicine. Voluntary medical expense insurance plans must be activated and provide a far wider coverage than they have so far done.

Medicine has survived and flourished since time immemorial because of its ability to adapt itself to changing circumstances. Its only difficulty lies now, not in its inability to change its modes of thinking or of practice upon proof of necessity, but in the *rate* at which it can move to accomplish change. It must be conscious of the public necessity; it must carefully study the effect of public necessity upon the acts and attitudes of government and prepare to fit itself into the rapidly changing social order in as short a period of time as this can be done and yet be consistent with public safety.—*N. Y. State J. M.*, Vol. 42, No. 18 (September).

MEDICAL EPONYMS

Plaut-Vincent's Angina

Hugo Carl Plaut (1858-1928), of Leipzig published his "Studien zur bacteriellen Diagnostik der Diphtherie und der Anginen [Studies in the Bacterial Diagnosis of Diphtheria and the Anginas]" in the *Deutsche medicinische Wochenschrift* (*20*:920-923, 1894). A portion of the translation follows:

"Five successive cases of simple angina deserve mention because of the type of microörganism that, there seems to be no doubt, was their cause. . . . Inspection of the oral cavity, which contained many carious teeth, showed a dirty exudate on both medial surfaces of the markedly swollen tonsils and the left side of the uvula. . . . Microscopic examination of the exudate showed it to consist bacteriologically of nothing but Miller's spirochetes and Miller's bacilli. . . . Miller's bacilli are . . . much larger than the diphtheria bacilli, are, in contradistinction to these, pointed at the ends, and are always associated with the spirochetes, which apparently have some genetic relation with them. . . . These microörganisms of Miller's are found in small numbers in almost every normal mouth, but usually only under the gum margins. [The organisms referred to were described by W. D. Miller, an American physician and dentist in Berlin, in 1883.]"

H. Vincent (1862), military surgeon and bacteriologist, wrote "Sur une forme particulière d'angine diphtéroïde (angine à bacilles fusiformes) [On a Peculiar Form of Diphtheroid Angina (Angina with Fusiform Bacilli)]" in the *Bulletins et mémoires de la société médicale des hôpitaux de Paris* (*15*, 3rd series: 244-250, 1898). A portion of the translation follows:

"This angina is characterized by a grayish or whitish pseudo-membranous exudate, by the associated fever and occasionally rather marked adenitis. . . .

"If a bit of the pulpy exudate that appears on the surface of the pharynx is removed and stained with thionin or Ziehl's dilute fuchsin, microscopic examination shows two kinds of microbes to be predominant: a peculiar bacillus, easily recognizable by its length (about 10 to 12 microns) and its bulging central portion and distinctly tapering ends, and a delicate spirillum, more difficult to stain. This spirillum is quite similar to that normally present in the saliva and dental tartar."—R. W. B., in *New England Journal of Medicine*.

"Never before have we had so little time in which to do so much."—Franklin D. Roosevelt.